

Fetal Intervention Increases Maternal T Cell Awareness of the Foreign Conceptus and Can Lead to Immune-Mediated Fetal Demise.

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Public Summary:

Fetal interventions to treat congenital anomalies are becoming standard treatment options, but often lead to preterm labor. The possible contribution of the maternal immune system to postsurgical pregnancy complications, particularly preterm labor leading to preterm delivery, has not been explored. We recently showed that fetal intervention in mice increases maternal T cell trafficking into the fetus and hypothesized that this process also may lead to increased maternal T cell recognition of the fetus and subsequent breakdown in maternal-fetal tolerance. In this study, we show that fetal intervention in mice results in accumulation of maternal T cells in the uterus and that these activated cells can produce effector cytokines--- small proteins that are released by cells and affect the behavior of other cells, and sometimes the releasing cell itself. We show that such activation and accumulation can have a functional consequence: in utero transplantation of hematopoietic cells carrying the fetal alloantigen leads to enhanced demise of semiallogeneic fetuses within a litter. We further show that maternal T cells are necessary for this phenomenon. These results suggest that fetal intervention enhances maternal T cell recognition of the fetus and that T cell activation may be a culprit in postsurgical pregnancy complications. Our results have clinical implications for understanding and preventing complications associated with fetal surgery such as preterm labor.

Scientific Abstract:

Fetal interventions to diagnose and treat congenital anomalies are growing in popularity but often lead to preterm labor. The possible contribution of the maternal adaptive immune system to postsurgical pregnancy complications has not been explored. We recently showed that fetal intervention in mice increases maternal T cell trafficking into the fetus and hypothesized that this process also may lead to increased maternal T cell recognition of the foreign conceptus and subsequent breakdown in maternal-fetal tolerance. In this study, we show that fetal intervention in mice results in accumulation of maternal T cells in the uterus and that these activated cells can produce effector cytokines. In adoptive transfer experiments, maternal T cells specific for a fetal alloantigen proliferate after fetal intervention, escape apoptosis, and become enriched compared with endogenous T cells in the uterus and uterine-draining lymph nodes. Finally, we demonstrate that such activation and accumulation can have a functional consequence: in utero transplantation of hematopoietic cells carrying the fetal alloantigen leads to enhanced demise of semiallogeneic fetuses within a litter. We further show that maternal T cells are necessary for this phenomenon. These results suggest that fetal intervention enhances maternal T cell recognition of the fetus and that T cell activation may be a culprit in postsurgical pregnancy complications. Our results have clinical implications for understanding and preventing complications associated with fetal surgery such as preterm labor.

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